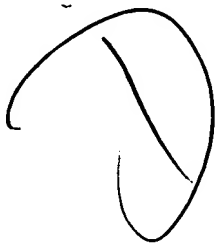

Appendix D

Krieg '388 Patent Claims Corresponding to Proposed Count 1

Applicants identify the following claims of the Krieg '388 patent as corresponding to proposed count 1. For the Examiner's convenience, the composition claims will be presented first, followed by the method claims. Applicants submit that the method claims are obvious in view of proposed count 1 directed to the immunostimulatory compositions and thus correspond to the count.

Composition claims

Claims 1-2, 4, 6-9. Claim 1 is directed to a composition comprising an antigen and an oligonucleotide sequence comprising an octameric sequence in which the dinucleotide sequence "TC" is 5' with respect to AACGTT, which is recited in both alternatives of proposed count 1. The claim recites that both C and G are unmethylated, which is a species within the recitation "wherein C is unmethylated". Applicants note that the base G is unmethylated, according to its chemical formula. As discussed above, (a) a plasmid renders an oligomer containing the same functional sequence obvious; and (b) an antigen is an obvious variant of an antigen encoded by a nucleic acid sequence of the plasmid (or, alternatively, if considered as a species of "antigen", an antigen encoded in a nucleic acid sequence anticipates "antigen"). Claims 2 and 4 are directed to compositions comprising an oligonucleotide sequence comprising hexameric, CG-containing sequences (wherein C and G are unmethylated) and an antigen. The hexameric sequences of claims 2 and 4 are species recited in the second alternative of proposed count 1.[10] The claims recite that both C and G are unmethylated, which is a species within the recitation "wherein C is unmethylated". Applicants note that the base G is unmethylated, according to its chemical formula. As discussed above, (a) a plasmid renders an oligomer containing the same functional

[10] Claim 2 recites 5'GACGTT3'; claim 4 recites 5'AACGCT3'.

sequence obvious; and (b) an antigen is an obvious variant of an antigen encoded by a nucleic acid sequence of the plasmid (or, alternatively, if considered as a species of "antigen", an antigen encoded in a nucleic acid sequence anticipates "antigen"). Claim 6 recites that the oligomer comprises a length between 8 and 100 nucleotides. A range of sizes for an oligomeric sequence is not patentably distinct from an "oligonucleotide sequence" as recited in claims 2 and 4. Claim 7 adds a "T" on the 5' end of the sequences of claims 1-5, which represents one of only four possibilities for that position. Claim 8 recites the oligonucleotide has a phosphate backbone modification. As discussed above, a phosphate backbone modification is obvious in view of a nucleic acid. Claim 9, which depends from claim 8, specifies an obvious type of phosphate backbone modification, namely a phosphorothioate backbone modification. Such a phosphate backbone modification was and is well-known in the art.

Claims 13-19, 22. Claim 13 is directed to a composition comprising an immunostimulatory CG-containing nucleic acid (as "$X_1X_2CGX_3X_4$", unmethylated C and G, X_1X_2 as any dinucleotide except X_1C, X_2X_4 as any dinucleotide except GX_4) having a phosphate backbone modification, with an antigen. With respect to the nucleic acid sequences encompassed by this claim, both alternatives of proposed count 1 anticipate these sequences by reciting a species within those sequences (AACGTT). As discussed herein, (a) a plasmid anticipates a nucleic acid; (b) an antigen is an obvious variant of an antigen encoded by a nucleic acid sequence of the plasmid (or, alternatively, if considered as a species of "antigen", an antigen encoded in a nucleic acid sequence anticipates "antigen"); and (c) a phosphate backbone modification is obvious in view of a nucleic acid. Claims 14-16 are dependent claims reciting Markush groups directed to various sequence species. Claim 14 recites (*inter alia*) that X_1X_2 can be AA and X_3X_4 can be TT, which is anticipated by proposed count 1 (AACGTT). Claim 15 recites (*inter alia*) that X_2 can be A, which is anticipated by proposed count 1 (AACGTT). Claim 16 recites (*inter alia*) that X_3 can be T, which is anticipated by proposed count 1

(AACGTT). Claim 17 recites that X_2 can be C or T,[11] which anticipated by the second alternative of proposed count 1. Claim 18 adds a "T" on the 5' end of the hexameric sequence, which represents one of only four possibilities for that position. Dependent claim 19 further adds two bases upstream of the "T" of claim 18, namely "TC". Dependent claim 22 recites a Markush group directed to species of X_2, all of which are recited in the second alternative of proposed count 1.

Method claim

Claim 21. Independent claim 21 is directed to a method for enhancing an immune response by administering a composition corresponding to claim 13[12] (discussed above) via enhancing B cell activation. This use of the composition of claim 13 is obvious in view of the composition. As discussed above, the Krieg '646 patent specification states that these compositions enhance the immune response.

Applicants submit that the above claims do not define separate patentable inventions within the meaning of 37 C.F.R. § 1.601(n).

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[11] Applicants note that claim 17, which recites that X_2 may be C, appears to lack antecedent basis in claim 13, which does not provide for any combination in which X_2 is a C.

[12] Claim 21 appears to have an error in that it recites that X_3X_4 can be GpT, which is excluded from claim 13. Otherwise, the polynucleotide permutations recited in claim 21 are identical to those of claim 13.